

REMARKS

Applicants have considered the Office Action mailed November 12, 2003 in connection with the above-identified patent application.

Drawings

The Examiner has pointed out an omitted reference sign from the drawings. Applicants transmit herewith, a "Replacement Sheet" with all figures from the immediate prior version of the sheet and an "Annotated Sheet Showing Changes," which are in an Appendix attached hereto. Accordingly, Applicants respectfully request the withdrawal of the objection and entry of the corrected drawing.

Amendments to Specification

Applicants have amended the specification to correct a number of typographical errors. It would be clear to one of ordinary skill in the art that each of these corrections would be inconsequential. Accordingly, Applicants assert that no new matter has been introduced and respectfully request their entry.

Amendments to the Claims

Claims 1-90 are pending in the instant Application. With the instant amendment, Applicants have amended claims 1-90, canceled claims 10, 16, 34, 36, 37, 76, and introduced new claims 91-134.

Claims 1-9, 11-15, and 17-19 have been amended to recite a "background electrolyte solution" rather than a "probe" and also to attend to various informalities of grammar and style.

The term "background electrolyte solution" has also been introduced into Applicants' remaining claims by the amendments herein.

Claim 1 has also been amended to recite a concentration of vinylogous carboxylic acid compounds, for example, as found in the specification as filed at page 11, lines 17-18. Claim 1 has been further amended to recite that the vinylogous carboxylic acid compound is not one of Applicants' disclosed species, tropolone. Since tropolone is a species disclosed by Applicants, Applicants are at liberty to exclude it from their claims. "It is for the inventor to decide what *bounds* of protection he will seek." *In re Johnson and Farnham*, 558 F.2d. 1008, 1018 (CCPA, 1977) (emphasis in original). Accordingly, Applicants assert that the

amendments to claims 1–19 find support in the specification as filed, and entry thereof is respectfully requested.

Claims 17 and 18 have been amended to recite an enol ester and an enol amide derivative respectively. Support for this limitation can be found in the specification as filed at page 10, line 11 to page 11, line 13, for example.

Claims 20–33, 35, 37, and 38 have been amended to attend to various informalities of grammar and style.

Claim 39 has been amended to recite a method of indirectly detecting ions in a sample and also to introduce a buffer. These amendments find support in the specification as filed at page 11, line 13, and at page 14, line 7, respectively, for example.

Claims 52 and 53 have been amended to recite an enol ester and an enol amide derivative respectively. Support for these amendments can be found in the specification as filed at page 10, line 11 to page 11, line 13, for example.

Claims 39–59 have also been amended to attend to various informalities of grammar and style.

Claim 60 has been amended to recite an apparatus for indirectly detecting ions in a sample and also to introduce a buffer. For instance, these amendments find support in the specification as filed at page 11, line 13, and at page 14, line 7, respectively.

Claims 73 and 74 have been amended to recite an enol ester and an enol amide derivative respectively, as discussed, for example, in the specification as filed at page 10, line 11 to page 11, line 13.

Claims 61–74 have also been amended to attend to various informalities of grammar and style.

Claim 75 has been amended to recite a kit for indirectly detecting ions in a sample and also to introduce a buffer. These amendments find support in the specification as filed at, for example, page 11, line 13, and at page 14, line 7, respectively.

Claims 89 and 90 have been amended to recite a enol ester, and enol amide derivative respectively, as discussed, for example, in the specification as filed at page 10, line 11 to page 11, line 13.

Claims 77–90 have also been amended to attend to various informalities of grammar and style.

New claims 91, 92, 98, 99, 106, 107, 114, and 115 recite limitations that the pH of the background electrolyte is within ranges disclosed in the specification as filed, for example, at page 11, lines 18–19.

New claims 93, 100, 108, 116, recite limitations that the buffer includes a base disclosed in the specification as filed, for example, at page 11, lines 15–16.

New claims 94, 95, 101, 109, 110, 117, 118, recite limitations that the background electrolyte also includes an electro-osmotic flow modifier, as disclosed in the specification as filed, for example, at page 11, lines 20–24.

New claims 96, 97, 103, 104, 111, 112, 119, 120 recite limitations that the background electrolyte also includes a solvent, as disclosed in the specification as filed, for example, at page 11, lines 24–26.

New claims 102, 105, 113, recite a limitation that the background electrolyte has a concentration of about 2 to 5 mM, as disclosed in the specification as filed, for example, at page 11, lines 17–18.

New claims 121, 123, and 125 recite, respectively, a method, apparatus, and kit, for performing indirect detection by capillary electrophoresis, wherein the background electrolyte comprises a vinylogous carboxylic acid compound which is not tropolone. Tropolone is one of Applicants' disclosed embodiments, and accordingly, as discussed hereinabove, Applicants are entitled to remove it from the scope of their claim. *In re Johnson and Farnham*, 558 F.2d. 1008, 1018 (CCPA, 1977).

Respective dependent claims 122, 124, and 126 recite a limitation that the vinylogous carboxylic acid is present in a concentration of about 2 to 5 mM. This limitation finds support in the specification as filed, for example, at page 11, lines 17–18.

Claims 124–131 have been introduced, each of which includes a limitation to a vinylogous carboxylic acid derivative compound having the structure, for example, found at pages 10 and 11 of the specification as filed.

Accordingly, no new matter is introduced by the claim Amendments presented herein, and entry thereof is respectfully requested.

FORMALITIES

Specification

In the Office Action dated November 12, 2003, the Examiner objected to the spelling of certain chemical compound names in the specification and also pointed out a typographical

error in the paragraph beginning on page 5, line 22. Applicants thank the Examiner for drawing attention to these issues and, accordingly, have amended relevant sections of the specification herein.

Objections to the Claims

In items 3 and 4 of the Office Action dated November 12, 2003, the Examiner enumerated grounds for objecting to a number of the claims. It is believed that with the amendments presented herein, Applicants have attended to these objections.

Applicants have identified one exception. At item 4.t., (at page 6 of the November 12, 2003 Office Action), the Examiner objected to “its concentration” and suggested an alternative form of language. Applicants believe that the term “the concentration” suggested by the Examiner would suffer from a lack of antecedent basis and, therefore, have not carried out the suggested Amendment. Applicants further believe that the wording of the claim as amended herein would be clear to one of ordinary skill in the art and accordingly respectfully request the Examiner’s reconsideration thereof.

REJECTIONS OF THE CLAIMS

Rejections under 35 U.S.C. § 112 (¶ 1)

The Examiner has rejected claims 1–90 under 35 U.S.C. § 112 (first paragraph) as allegedly being based on a non-enabling disclosure. Applicants respectfully traverse the rejection.

First, the Examiner has alleged that the scope of the claims exceeds that of the disclosure because, according to the Examiner, only those vinylogous carboxylic acid compounds as defined in the specification are properly enabled. In particular, the Examiner concludes from Applicants’ definition of a vinylogous carboxylic acid compound found on pages 6 and 10 of the specification that the specification “does not reasonably provide enablement for *any* vinylogous carboxylic acid compound.” November 12, 2003 Office Action, at page 7 (emphasis added).

Applicants believe that the definition of a vinylogous carboxylic acid compound recited in the specification is consistent with the definition that would be understood by one of ordinary skill in the art. Indeed, Applicants provide herewith, in connection with an Information Disclosure Statement, a copy of a literature reference (G.V. Perez and Alice L.

Perez, “Organic Acids without a Carboxylic Acid Functional Group”, *J. Chem. Ed.*, Vol. 77, No. 7, July 2000, pgs. 910-915; hereinafter, “Perez”) that discusses vinylogous carboxylic acids. In particular, Perez states that “[t]he juxtaposition of a hydroxy group in conjugation with a carbonyl can be thought of as a ‘vinylogous carboxylic acid’”. (Perez, p.911, at bottom of left hand column.) Further examples of vinylogous carboxylic acids are provided in Perez (see pages 911–912), all of which are consistent with the species disclosed in Applicants’ specification.

Accordingly, one of ordinary skill in the art would appreciate that the term “vinylogous carboxylic acid compound” as recited in Applicants’ claims would be consistent with the definition provided in Applicants’ specification. Therefore, Applicants respectfully submit that the specification is fully enabling for the claimed compounds.

The Examiner has additionally questioned Applicants’ use of the terms “ester derivative” or “amide derivative” of vinylogous carboxylic acid compounds. Although Applicants believe that one of ordinary skill in the art would find such a term to be clear, in an effort to expedite prosecution, Applicants have amended the pertinent claims herein to specify an “enol” ester derivative.

Second, the Examiner has alleged that claims 1–90 are not reasonably enabling for vinylogous carboxylic acid compounds “having little UV absorptivity”. Again, Applicants respectfully point out that their definition of a vinylogous carboxylic acid compound is consistent with what would be understood by one of ordinary skill in the art. Such compounds have an enol group in conjugation with a carbonyl group and thus contain a chromophore that is UV absorbing. To support this point, Applicants provide herewith, as an attached exhibit, an excerpt from a standard work of organic chemistry (Allinger, *et al.*, *Organic Chemistry*, 2nd Ed., (1976), at pages 764–768). This reference establishes that groups such as carbonyl and vinyl absorb in the UV and that conjugated systems including those groups also have characteristic UV absorption bands. As acknowledged by the Examiner, and as presented in Applicants’ specification as filed, these groups are present in all vinylogous carboxylic acids. Thus, Applicants are unable to appreciate what vinylogous carboxylic acid compounds in particular would be lacking in UV absorptivity.

Accordingly, Applicants respectfully submit that claims 1–90 are properly enabled by the specification as filed and request that the Examiner remove the rejection of record.

Rejections under 35 U.S.C. § 112 (¶ 2)

The Examiner has rejected claims 14, 17–19, 33, 35, 37, 52, 53, 57, 73, 74, 89, and 90 under 35 U.S.C. § 112 (second paragraph) as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants have amended claims 14, 17–19, 33, 35, 52, 53, 57, 73, 74, 89, and 90, and believe that the rejections are now moot.

In particular, claims 14 and 33 now recite the limitation that the vinylogous carboxylic acid compound “has a peripheral substituent that does not alter its vinylogous carboxylic acid UV-chromophore”. The term “group of vinylogous compounds” has also been amended in claim 33.

Claims 17, 52, 73, and 89 have been amended herein so that they properly limit the claims from which they respectively depend. Claims 18, 53, 74, and 90 have been similarly amended.

The Examiner has not articulated a specific reason for issuing a rejection of claim 19 under 35 U.S.C. § 112 (second paragraph) but, with this amendment, Applicants have amended claim 19 to depend from claim 1 and to correct various aspects of grammar and style.

Claim 57 now recites cations that are “selected from the group consisting of: Na^+ , K^+ , Mg^{+2} , Ca^{+2} , and small molecular weight organic cations” in place of the language objected to by the Examiner so that the Examiner’s articulated rejection is now moot.

The preambles of claims 33, 35 and 37 have all been amended, as has the preamble to claim 1, so that proper antecedent basis is now present.

Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 112 (second paragraph) be removed.

Rejections under 35 U.S.C. § 102(b)

Examiner has rejected claims 1-16, 18-26, 32-37, 39-42, 48, 51, 55, 60-63, 69, 72, 75-88, and 90 under 35 U.S.C. § 102(b) as allegedly being anticipated by one or more of several references. Applicants respectfully traverse these rejections.

With the instant amendment, Applicants have amended claim 1 to recite a solution in which the probe concentration of about 2 to 5 mM, and in which the vinylogous carboxylic acid compound excludes tropolone. Independent claims 20, 39, 60 and 75 have been

amended so that the background electrolyte comprises a buffer, and so that the respective preambles recite “indirectly detecting ions”.

The rejection over Oehrle

Examiner has rejected claims 1–4, 10, 13–16, 19, 39–42, 48, 51, 55, 60–63, 69, 72, 75, 77–79, 85 and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by Oehrle, “Controlled changes in selectivity of cation separations by capillary electrophoresis using various crown-ether additives,” *J. Chromatogr. A*, 745, (1996), 87-92 (“Oehrle”, hereinafter). Applicants respectfully traverse the rejection.

Oehrle teaches ion separation by capillary electrophoresis, in which ion detection is accomplished through indirect UV detection and the use of an electrolyte containing tropolone in a concentration of 3.0 mM (Oehrle, pages 87-88). However, the electrolyte solution of Oehrle does not contain a buffer.

Applicants’ claim 1 excludes tropolone as one of the vinylogous carboxylic acid compounds used in the background electrolyte solution. Accordingly, Oehrle does not anticipate claim 1, or any claim depending therefrom, because Oehrle only teaches the use of tropolone.

Applicants’ independent claims 39, 60, and 75 all recite a buffer. Thus, Oehrle does not anticipate these claims or any claim depending therefrom because Oehrle does not teach the use of a buffer.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1-4, 10, 13–16, 19, 39–42, 48, 51, 55, 60–63, 69, 72, 75, 77–79, 85 and 88 over Oehrle.

The rejection over Tu

Examiner has rejected claims 1–7, 13–16, 19–26, 32-37, 75–82, and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by Tu *et al.*, “The influence of fluorescent dye structure on the electrophoretic mobility of end-labeled DNA,” *Nucleic Acids Research*, 1998, Vol. 26, No. 11, 2797-2802 (hereinafter “Tu”). Applicants respectfully traverse the rejection.

Tu teaches the use of capillary electrophoresis to detect charged molecules, in which squaric acid derivatives are used in an unspecified concentration for direct fluorescence detection of DNA samples (Tu, pages 2797–2798).

With respect to Applicants' claim 1, Tu does not specify a concentration range of about 2 to 5 mM for any of the listed squaric acid derivatives. Accordingly Tu does not anticipate claim 1, or any claim depending therefrom, because it does not disclose the recited concentration.

Additionally, Applicants' claims 20 and 75 recite a background electrolyte solution for indirect detection in capillary electrophoresis. Therefore, Tu does not anticipate independent claims 20 and 75, or any claim depending therefrom, because it does not teach a method of indirect detection but instead relies upon direct detection, which is fluorescence of the electrolyte chemicals.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1-7, 13-16, 19-26, 32-37, 75-82, and 88 over Tu be removed.

The rejection over Gadek

The Examiner has rejected claims 1-4, 7, 13, 14, 75, 77-79, 82, and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,104,308 to Gadek, *et al.*, ("Gadek"). Applicants respectfully traverse the rejection.

Gadek merely teaches synthesis of squaric acid (col.1, lines 5-13), but no solution containing squaric acid, with or without a buffer, or application thereof to indirect ion detection by capillary electrophoresis.

Claim 1 recites a background electrolyte solution containing a vinylogous carboxylic acid compound in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom, is anticipated by Gadek, which is silent as to concentration.

Claim 75 recites a kit comprising a vinylogous carboxylic acid compound and a buffer. Therefore, Gadek does not anticipate claim 75 or any claim depending therefrom because Gadek does not teach or disclose a buffer. Furthermore, rather than teaching a kit for capillary electrophoresis, Gadek teaches a method of synthesis.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 2-4, 7, 13, 14, 77-79, 82, and 88 over Gadek.

The rejection over Weinberg

The Examiner has rejected claims 1-4, 7, 8, 13, 14, 75, 77-79, 82, 83, and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,478, 694 to Weinberg ("Weinberg"). Applicants respectfully traverse the rejection.

Weinberg merely teaches the electrosynthesis of polyols, in particular to ethylene glycol (Weinberg, col. 3, lines 3–10). Weinberg refers to squaric acid, 2,5-dihydroxy-p-benzoquinone, and rhodizonic acid as “oxygenated derivatives” that are present in a solution. Neither of these compounds is present in a concentration that is in the range of 2 to 5 mM.¹ Furthermore, Weinberg does not teach detection of ions by capillary electrophoresis, or a background electrolyte containing a vinylogous carboxylic acid compound and a buffer.

Claim 1 recites a background electrolyte solution containing a vinylogous carboxylic acid compound in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom is anticipated by Weinberg, which does not disclose a solution containing a vinylogous carboxylic acid in the recited concentration.

Claim 75 recites a kit comprising a vinylogous carboxylic acid compound and a buffer. Therefore, Weinberg does not anticipate claim 75 or any claim depending therefrom because Weinberg does not teach a buffer, and also because Weinberg teaches methods of electrosynthesis, and not a kit for capillary electrophoresis.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1–4, 7, 8, 13, 14, 75, 77–79, 82, 83, and 88 over Weinberg.

The rejection over Brois

Claims 1–6, 9, 13, 14, 16, 75, 77–81, 84, and 88 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,288,811 to Brois (“Brois”). Applicants respectfully traverse the rejection.

Brois teaches cyclic carbonyl containing compounds and methods of preparing the same. Amongst the compounds disclosed by Brois are croconic acid, and rhodizonic acid. Brois does not teach a vinylogous carboxylic acid compound in a concentration of about 2 to 5 mM. Neither does Brois teach or disclose ion detection by capillary electrophoresis or a background electrolyte containing a vinylogous carboxylic acid and a buffer.

Claim 1 recites a background electrolyte solution containing a vinylogous carboxylic acid compound in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom is anticipated by Brois, which does not disclose a solution containing a vinylogous carboxylic acid in the recited concentration.

¹ Weinberg recites that the oxygenated derivatives are present at concentrations of 1g / 100 ml (Weinberg, Col.12, lines 45–47). For 2,5-dihydroxy-p-benzoquinone, rhodizonic acid, and squaric acid, (whose respective molecular weights are 190, 170, and 114), these concentrations are respectively 53 mM, 59 mM, and 88 mM.

Claim 75 recites a kit comprising a vinylogous carboxylic acid compound and a buffer. Therefore, Brois does not anticipate claim 75 or any claim depending therefrom because Brois teaches cyclic carbonyl containing compounds and methods of preparing the same, not a buffer or a kit for capillary electrophoresis.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1–6, 9, 13, 14, 16, 75, 77–81, 84, and 88 over Brois.

The rejection over Theodoropulos

Examiner has rejected claims 1–4, 10, 13, 14, 16, 18, 75, 77–79, 85, 88, and 90 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,215, 890 to Theodoropulos, *et al.*, (“Theodoropulos”). Applicants respectfully traverse the rejection.

Theodoropulos teaches the preparation and use of a chromogenic substrate to peroxidase, which is used to determine peroxidase in biological substances (Theodoropulos col. 2, lines 44-47). Theodoropulos discloses a cationic derivative of tropolone (Theodoropulos, structure V at Col. 3). The Examiner has characterized this structure as a “cationic amide derivative”. However, the structures recited in claims 18 and 90, as amended herein, are enol amide derivatives and are therefore distinct from the structures disclosed in Theodoropulos.

Furthermore, Theodoropulos does not teach ion detection by capillary electrophoresis, or a background electrolyte containing a vinylogous carboxylic acid compound. Theodoropulos teaches (Example 5, Col. 6, lines 43–51) a buffered solution of “2-hydroxy-2,4,6-cyclohepta-Trienone” (tropolone) but its concentration is 8 mM (based on a molecular weight of 122 for tropolone), and the solution is not a background electrolyte.

Claim 1 recites a background electrolyte solution containing a vinylogous carboxylic acid compound, excluding tropolone, in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom is anticipated by Theodoropulos, which only discloses tropolone and in a concentration outside of the recited range.

Claim 75 recites a kit comprising a vinylogous carboxylic acid compound and a buffer. By contrast, Example 5 of Theodoropulos is not a kit, but instead is a reagent solution that has been prepared for a subsequent reaction to produce a dye. Therefore, Theodoropulos does not anticipate claim 75 or any claim depending therefrom because Theodoropulos does not teach a kit for capillary electrophoresis.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1–4, 10, 13, 14, 16, 18, 75, 77–79, 85, 88 and 90 over Theodoropoulos.

The rejection over McClune

The Examiner has also rejected claims 1–4, 11, 13, 14, 16, 20–23, 30, 32, 33, 35, 75–79, 86, and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Pat. No. 4,828,983 to McClune (“McClune”). Applicants respectfully traverse the rejection.

McClune teaches an analyte determination method that utilizes a leuco dye, which provides a detectable dye in the presence of peroxidase and hydrogen peroxide, and a phenol or aniline electron transfer agent that is capable of reacting with hydrogen peroxide in the presence of peroxidase to provide an intermediate compound which has a higher oxidation potential than the leuco dye (col. 2, line 21 to col. 3, line 16). The only recitation of a vinyllogous carboxylic acid compound in McClune is a reference to a 0.05 molar sample of dimedone pointed out by the Examiner (McClune, Example 3, at Col. 10, line 36). This solution is buffered but it is not a background electrolyte for capillary electrophoresis. Furthermore, McClune does not teach indirect ion detection by capillary electrophoresis.

Claim 1 recites a background electrolyte solution containing a vinyllogous carboxylic acid compound, in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom is anticipated by McClune, which discloses a solution of dimedone in a concentration outside of the recited range.

Claim 20 recites a background electrolyte solution for capillary electrophoresis, comprising a vinyllogous carboxylic acid compound and a buffer. Thus neither claim 20 nor any claim depending therefrom is anticipated by McClune, because McClune discloses a buffered solution that is for use as an electron-transfer agent (McClune, col. 10, lines 28–37). One of ordinary skill in the art would appreciate that a composition suitable for use as an electron transfer agent would not be suitable for use as a background electrolyte for capillary electrophoresis.

Claim 75 recites a kit comprising a vinyllogous carboxylic acid compound and a buffer. By contrast, Example 3 of McClune is not a kit, but instead is a reagent solution that has been prepared for increasing the reaction rate of peroxidase. Therefore, McClune does not anticipate claim 75 or any claim depending therefrom because McClune does not teach a kit for capillary electrophoresis.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1–4, 11, 13, 14, 16, 20–23, 30, 32, 33, 35, 75, 76–79, 86, and 88 over McClune.

The rejection over Franke

The Examiner has also rejected claims 1–4, 12, 13, 14, 16, 75, 77–79, 87, and 88 under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,340,595 to Franke *et al.* (“Franke”). Applicants respectfully traverse the rejection.

Franke teaches the use and preparation of aminopropanol derivatives of 6-hydroxy-2,3,4,5-tetrahydro-1H-1-benzazepin-2-one, in the context of pharmaceutical formulations, such as cardiac and circulatory drugs (Franke, Abstract). Franke does not teach indirect ion detection by capillary electrophoresis, or a background electrolyte containing a vinylogous carboxylic acid compound with or without a buffer. The only reference to a vinylogous carboxylic acid compound is that referenced by the Examiner, to 6-hydroxy-tetralone (Franke, Col. 6, line 27). However, this reference is only the compound when used as a starting material for a synthesis of 2,3,4,5-tetrahydro-1H-1-benzazepin-2-one.

Applicants’ Claim 1 recites a background electrolyte solution containing a vinylogous carboxylic acid compound, in a concentration of about 2 to 5 mM. Thus, neither claim 1 nor any claim depending therefrom is anticipated by Franke, which fails to disclose a solution of a vinylogous carboxylic acid in a concentration within the recited range.

Claim 75 recites a kit comprising a vinylogous carboxylic acid compound and a buffer. Therefore, Franke does not anticipate claim 75 or any claim depending therefrom because Franke teaches neither a kit for capillary electrophoresis, nor a buffer.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) of claims 1–4, 12, 13, 14, 16, 75, 77–79, 87, and 88 over Franke.

New Claims

As noted hereinabove, Applicants have added new claims 91–134 with the instant amendment. Claims 91–120 and 124–131 are dependent upon claims 1–90, and therefore incorporate limitations from them. Accordingly, claims 91–120 and 127–134 are allowable over each of the references cited by the Examiner in support of a rejection under § 102(b) of one or more of claims 1–90.

New independent claims 121, 123, and 125, and claims depending therefrom, include limitations that recite to indirectly detecting ions and a background electrolyte “containing one or more probes that is a vinylogous carboxylic acid compound, wherein the vinylogous carboxylic acid compound is not tropolone.” Therefore, the references cited hereinabove do not anticipate claims 121, 123, and 125 or any claims depending therefrom because none of these references contain all of the recited limitations.

Rejections under 35 U.S.C. § 103

The U.S. Patent and Trademark Office (“PTO”) bears the burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). To establish a *prima facie* case, the PTO must satisfy three basic criteria. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the reference teachings in the manner suggested by the PTO. *In re Rouffet*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998). Second, the skilled artisan, in light of the teachings of the prior art, must have a reasonable expectation that the modification or combination suggested by the PTO would be successful. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Finally, the prior art reference, or references when combined, must teach or suggest each and every limitation of the claimed invention. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The teaching or suggestion to make the claimed invention and the reasonable expectation of success must both be found in the prior art, not in the Applicant’s disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). If any one of these criteria is not met, *prima facie* obviousness is not established.

The rejection over Oehrle in view of What is Life

The Examiner has rejected claims 5–9, 11, 12, 17, 18, 43–47, 49, 50, 52, 53, 57, 64–68, 70, 71, 73, 74, 80–84, 86, 87, 89, and 90, under 35 U.S.C. § 103(a) as allegedly being obvious over *Oehrle*, in view of <http://www.whatislife.com/reader/dna-ma/dna-ma.html> (“*What is Life*”). Applicants respectfully traverse the rejection on the grounds that the references in combination do not provide each and every element of Applicants’ claimed invention, and also because the teachings of *What is Life* do not provide sufficient basis for

one of ordinary skill in the art to choose compounds other than tropolone for indirect ion detection by capillary electrophoresis.

First, Applicants respectfully point out that claim 1 as amended herein provides for a solution that contains a vinylogous carboxylic acid that is not tropolone. Thus, claims 5–9, 11, 12, 17, and 18 which depend therefrom are similarly limited. Accordingly, the combined teachings of Oehrle and What is Life do not teach or recite each and every limitation of claims 5–9, 11, 12, 17, and 18.

Second, claims 39, 60, and 75 as amended herein recite a background electrolyte solution that contains a vinylogous carboxylic acid and a buffer. Thus, claims 43–47, 49, 50, 52, 53, 57, 64–68, 70, 71, 73, 74, 80–84, 86, 87, 89, and 90, which individually depend therefrom, are similarly limited. Neither Oehrle nor What is Life teaches or discloses a buffer for use in capillary electrophoresis. Therefore, the combination of Oehrle and What is Life fails to teach or disclose every limitation of claims 5–9, 11, 12, 17, 18, 43–47, 49, 50, 52, 53, 57, 64–68, 70, 71, 73, 74, 80–84, 86, 87, 89, and 90.

Furthermore, as acknowledged by the Examiner, the combination of Oehrle and What is Life does not teach or suggest each and every limitation of the claimed invention because What is Life does not explicitly disclose the vinylogous carboxylic acid compounds recited in the rejected claims. Thus, the basis of the rejection is the Examiner's view that What is Life provides sufficient teaching of UV absorbance data to permit one of ordinary skill in the art to substitute other compounds for tropolone in the capillary electrophoresis method of Oehrle. Applicants respectfully disagree that What is Life provides such a teaching.

What is Life describes the structure of deoxyribonucleic acid (DNA), and, in passing, references the characteristic UV absorption band of aromatic ring structures (260 nm). What is Life is silent about UV absorption for other compounds, conspicuously the vinylogous carboxylic acid compounds of Applicants' invention, and in particular the hetero-atom containing compounds in claims 5, 6, 43, 44, 64, 65, 80, and 81, the specific vinylogous carboxylic acid compounds of claims 7–9, 11, 12, 45–47, 49, 50, 66–68, 70, 71, 82–84, 86, and 87, and the cationic ester and amide derivatives of claims 17, 18, 52, 53, 73, 74, 89 and 90. It is also worth emphasizing that none of the vinylogous carboxylic acid compounds recited in claims 7–9, 11, 12, 45–47, 49, 50, 66–68, 70, 71, 82–84, 86, and 87 is an aromatic compound. Furthermore, claim 57 as amended herein makes no reference to specific compounds for use in capillary electrophoresis. Accordingly, the combination of Oehrle and

What is Life provides no teaching or suggestion to direct one of ordinary skill in the art to any of Applicants' recited compounds.

Accordingly, Applicants respectfully submit that claims 5–9, 11, 12, 17, 18, 43–47, 49, 50, 52, 53, 57, 64–68, 70, 71, 73, 74, 80–84, 86, 87, 89, and 90 are not obvious over a combination of Oehrle and What is Life, and request that the rejection be withdrawn.

The rejection over Oehrle in view of Jones

The Examiner has rejected claims 20–23, 29, 32–38, 54, 56, 58, 59, and 76 under 35 U.S.C. § 103(a) as allegedly being obvious over Oehrle in view of U.S. Patent No. 5,128,005 to Jones, *et al.* ("Jones"). Applicants respectfully traverse the rejection.

With respect to claims 20–23, 29, and 32, 33, 35, 38, 54, 56, 58, 59 and 76 (claims 34, 36 and 37 having been canceled herein), Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness.

Claims 20–23, 29, and 32, 33, 35, 38, 54, 56, 58, 59 and 76 recite a background electrolyte solution for capillary electrophoresis which contains a vinylogous carboxylic acid compound in conjunction with a buffer.

As mentioned hereinabove, Oehrle teaches cation separation by capillary electrophoresis, in which indirect ion detection is accomplished through UV absorption and an electrolyte containing tropolone. The electrolyte solution of Oehrle does not contain a buffer. Jones teaches a method for separating cations or anions in solution by capillary electrophoresis using indirect UV detection (Jones, col 2, lines 29–32), but instead of tropolone, uses an inorganic salt of a UV-absorbing anion (*e.g.*, iodide, tungstate, molybdate, chromate, ferrocyanide, ferricyanide, or vanadate) (Jones, col. 2, lines 52–56). Jones also teaches the use of organic, aromatic carboxylic acid, compounds for separating anions (Jones, col. 5, lines 50–60) but suggests that they are less preferred. Jones teaches use of other UV absorbing organic compounds for separating cations but none of these is a vinylogous carboxylic acid. Jones also discloses the use of buffers generally in capillary electrophoresis (col. 1, lines 30–42) but without specific reference to the situations in which they are employed.

One of ordinary skill in the art would not have been motivated to combine the teachings of Oehrle and Jones because Oehrle is directed to separations of cations, whereas Jones is principally directed to separation of anions, and the teaching that pertains to cations utilizes compounds that are very different from tropolone. The compounds taught by Jones

for use in cation separation are: 4-methyl-benzylamine, 2-aminopyridine, 2-amino-4,6-dimethyl-pyridine, MES, 3-[(3-cholamidopropyl)dimethylammonio]-1-propane sulfonate (CHAPS), and N-[2-hydroxyethyl]piperazine-N'-[3-propane sulfonic acid] (EPPS) (Jones, Col.6, line 62 – col.7, line 1). None of these is a vinylogous carboxylic acid and none is structurally similar to tropolone. Thus, because of these differences in chemistry, one of skill in the art would not have been motivated to combine Oehrle and Jones to arrive at Applicants' claimed invention.

Additionally, neither reference provides a specific teaching that a buffer solution should be used in conjunction with a vinylogous carboxylic acid compound. Although Oehrle discloses tropolone, it makes no reference to a buffer. Jones, on the other hand, discloses species that are structurally distinct from tropolone and other vinylogous carboxylic acids and its reference to a buffer is only in the most general of terms. Therefore, one of ordinary skill in the art, in possession of the teachings of Oehrle and Jones would not have been motivated to use a buffer in conjunction with a vinylogous carboxylic acid compound.

Furthermore, with respect to claims 32 and 33, neither Oehrle nor Jones teaches any of the recited vinylogous carboxylic acid compounds or substituted forms thereof with any specificity. Thus, the combination of Oehrle and Jones fails to teach or suggest every limitation of claims 32 and 33.

Accordingly, Applicants respectfully submit that none of claims 20–23, 29, 32, 33, 35, 37, 38, 54, 56, 58, 59, and 76 is obvious over a combination of Oehrle in view of Jones, and request that the rejection be withdrawn.

The rejection over Oehrle in view of Jones and What is Life

The Examiner has rejected claims 24–28, 30, and 31 under 35 U.S.C. § 103(a) as allegedly being obvious over Oehrle in view of Jones, and further in view of What is Life. Applicants respectfully traverse the rejection.

The Examiner bases his rejection upon his combination of Oehrle and Jones, as discussed hereinabove, and further upon his allegation that one of ordinary skill in the art in possession of the teachings of What is Life would have been motivated to choose the compounds recited in claims 24–28, 30 and 31 for use in capillary electrophoresis. For the reasons articulated hereinabove, Applicants again respectfully disagree.

Applicants respectfully remind the Examiner that to establish a *prima facie* case of obviousness, all of the claim limitations must be taught or suggested by the prior art. In re

Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The Examiner acknowledges that the combination of Oehrle and What is Life does not teach or suggest each and every limitation of the rejected claims because neither reference discloses the recited vinylogous carboxylic acid compounds. These deficiencies are not provided by Jones, and, furthermore, for reasons discussed hereinabove, What is Life is conspicuously silent about UV absorption for the vinylogous carboxylic acid compounds of Applicants' invention and therefore does not provide one of ordinary skill in the art a basis upon which to choose vinylogous carboxylic acid compounds.

Accordingly, Applicants respectfully submit that claims 24–28, 30, and 31 are not obvious over a combination of Oehrle in view of Jones, and What is Life, and request that the rejection be withdrawn.

The rejection over Tu in view of Jones

Finally, the Examiner has rejected claims 60–66 and 72 under 35 U.S.C. § 103(a) as allegedly being obvious over Tu in view of Jones. Applicants respectfully traverse the rejection.

Claims 60–66, and 72 recite a capillary electrophoresis apparatus for indirectly detecting ions, using a background electrolyte containing a vinylogous carboxylic acid.

As discussed hereinabove, Tu teaches a method of carrying out capillary electrophoresis in which squaric acid derivatives provide a means for direct detection of DNA fragments by fluorescence. Jones teaches a method of separating ions by capillary electrophoresis using indirect UV detection but does not disclose using vinylogous carboxylic acid derivatives. The Examiner has alleged that the combination of Tu and Jones renders Applicants' claimed invention obvious because, although Tu does not disclose UV detection, Jones does. Applicants respectfully disagree with the Examiner's conclusion.

Although Tu discloses squaric acid derivatives, Tu provides no reason to suppose that they could be used in an indirect detection method. Similarly, Jones provides no teaching that squaric acid derivatives or any other vinylogous carboxylic acid compounds could be used in an indirect detection method. Accordingly, one of ordinary skill in the art would not have been motivated to use the compounds of Tu in the method of Jones, or the method of detection in Jones in conjunction with that of Tu without some specific indication that the compounds in question could be appropriately detected.

Furthermore, with respect to claims 66 and 72, neither Tu nor Jones discloses any of the recited compounds. Thus, the combination of Tu and Jones fails to teach or disclose all of the limitations of the rejected claims.

Accordingly, Applicants respectfully submit that none of claims 60-66, and 72 is obvious over a combination of Tu in view of Jones, and request that the rejection be withdrawn.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the subject application is in good and proper order for allowance. Withdrawal of the Examiner's rejections and early notification to this effect are earnestly solicited.

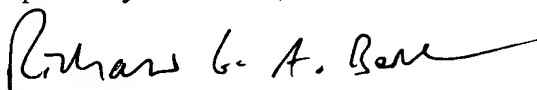
If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 4393-4935.

No fee is believed owed in connection with filing of this amendment and response. However, should the Commissioner determine otherwise, the Commissioner is authorized to charge any underpayment or credit any overpayment to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 (order no. 60825-5003) for the appropriate amount. A copy of this sheet is attached.

Respectfully submitted,

Date: May 12, 2004

By: _____



Richard G. A. Bone
Limited Recognition Under 37 C.F.R. § 10.9(b)
(Copy of Certificate attached hereto)

for David R. Owens, Reg. No. 40,756
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APPENDIX:
Amendments to the Drawings
And
Copy of Excerpt from Allinger *et al.*, *Organic Chemistry*

REPLACEMENT SHEET

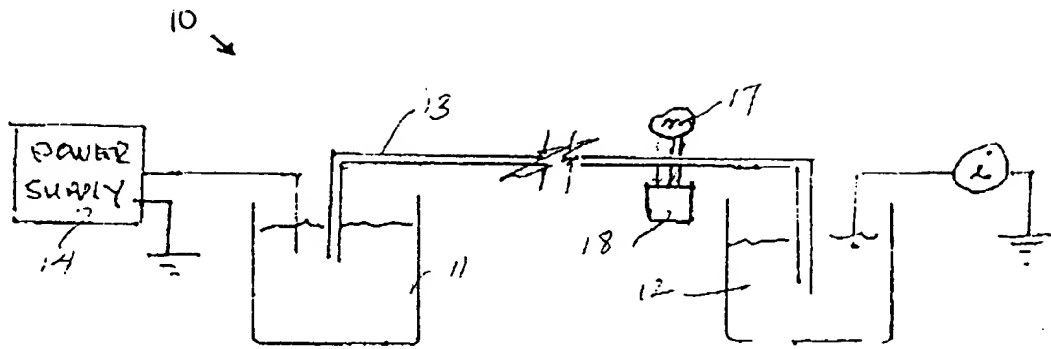


FIGURE 1

ANNOTATED SHEET SHOWING CHANGES

- PLEASE ADD REFERENCE NUMBER "10" WITH AN ARROW POINTING GENERALLY AT THE CE SYSTEM, AS SHOWN BELOW.

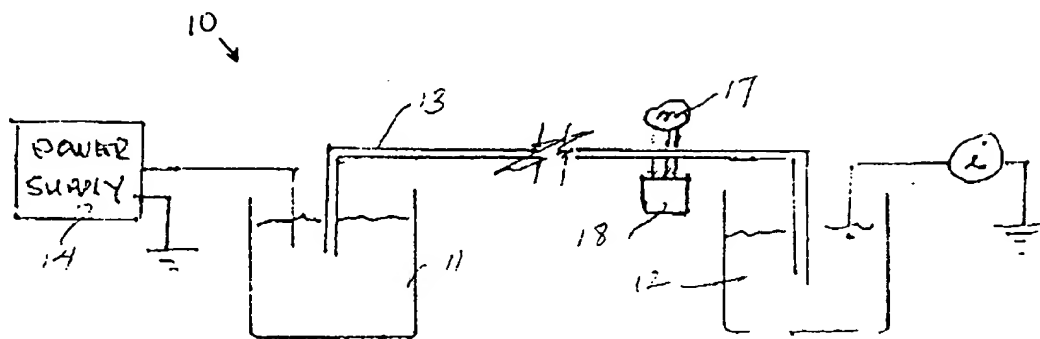


FIGURE 1